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Successful Treatment of a Patient With Cardiac Lymphoma Who Presented With a Complete Atrioventricular Block

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A patient with primary cardiac lymphoma, which is very rare, generally is regarded to have a poor prognosis. We herein report a patient with cardiac lymphoma who was treated successfully by systemic chemotherapy and radiotherapy using a pacemaker to control the complete atrioventricular (A-V) block. A 70-year-old man had a syncope caused by a complete A-V block. An echocardiogram, a computed tomographic scan, and magnetic resonance imaging of his chest showed a cardiac tumor. At this time, a biopsy of the cardiac tumor disclosed malignant lymphoma (diffuse large cell type, B cell type). The patient was thus treated with systemic chemotherapy and radiotherapy and, as a result, achieved a complete remission with a disappearance of the A-V block. Recently, several successful outcomes involving primary cardiac lymphoma have been reported because of the progress in diagnostic techniques including echocardiography, computed tomographic scanning, and magnetic resonance imaging, as well as improvement in the therapy of malignant lymphoma. Our clinical experience indicated that an early and accurate diagnosis combined with the appropriate therapy can thus help in obtaining a long survival in patients with primary cardiac lymphoma. Am. J. Hematol. 59:171–174, 1998. © 1998 Wiley-Liss, Inc.

Key words: cardiac lymphoma; A-V block

INTRODUCTION

Malignant lymphoma rarely involves the heart at initial diagnosis, although cardiac involvement, as a part of disseminated malignant lymphoma, late in the course of the illness appears to be more common, and cardiac involvement has been observed in nearly 20% of all cases who undergo an autopsy [1–3]. Most of the reported cardiac lymphoma patients died before specific therapy could be instituted because they could not be diagnosed accurately and thus tended to demonstrate a poor prognosis. However, the successful treatment of several cases with cardiac lymphoma, who were accurately diagnosed, have been reported recently [4–7].

We herein describe a patient with cardiac lymphoma who was treated successfully by systemic chemotherapy and radiotherapy. The pacemaker was used to control the arrhythmia which was inadvertently induced by lymphoma cell infiltration.

CASE REPORT

A 70-year-old Japanese man was admitted to the Tokushukai Hospital in Fukuoka because of palpitation in May, 1994. An electrocardiogram (ECG) showed paroxysmal atrial fibrillation. The atrial fibrillation disappeared after the administration of disopyramide. He was

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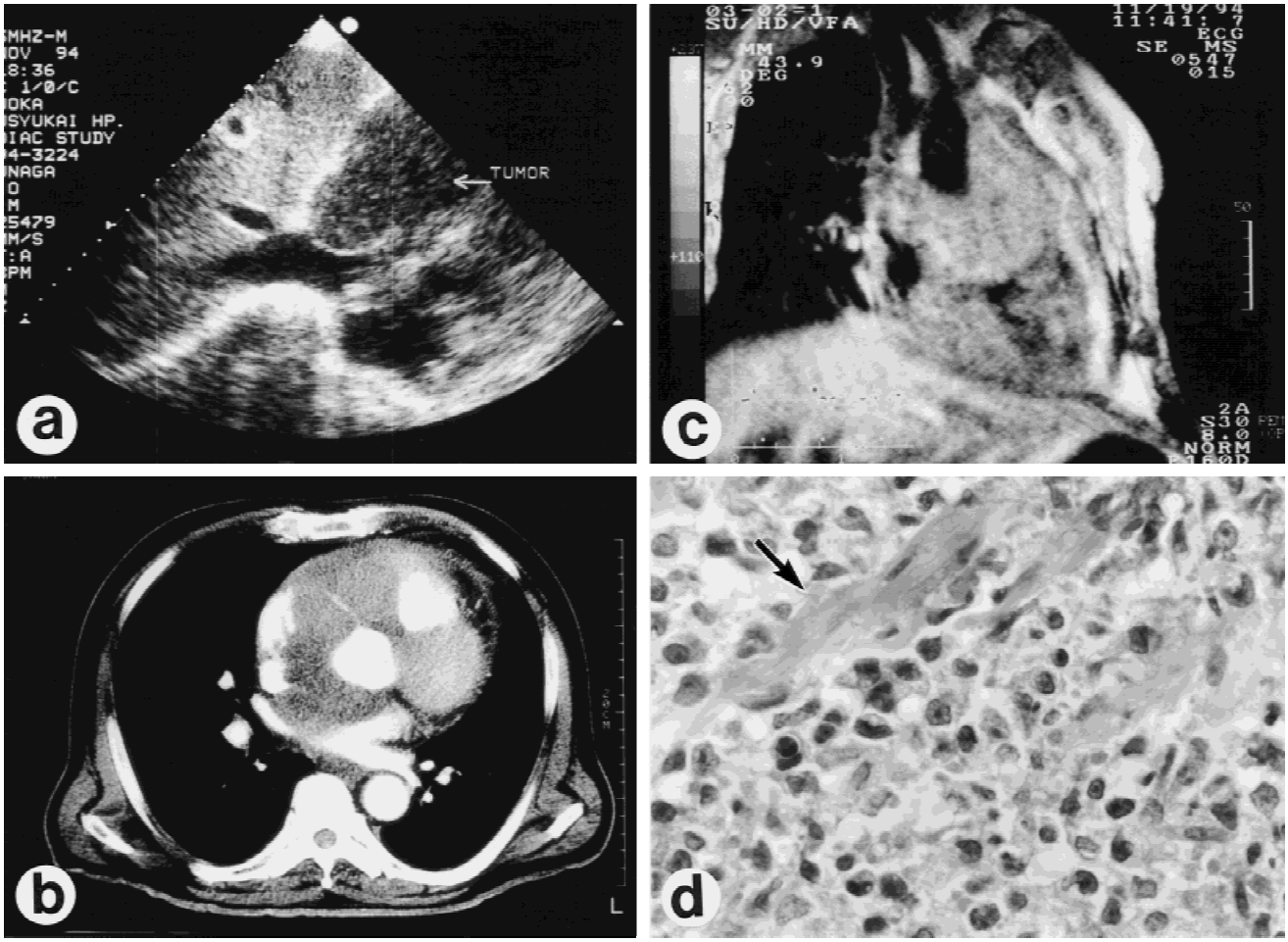

Fig. 1. a: A two-dimensional echocardiogram shows a large atrioventricular tumor; b: An axial image from computed tomography showing a low-density mass in the right atrioventricular region; c: Sagittal views from magnetic resonance imaging of the heart displaying a mass in the right atrioventricular region; and d: A biopsy specimen of the cardiac tumor (H & E stain). A diffuse proliferation of large lymphoid cells is observed. A few degenerated fibers of the myocardium are also scatteringly observed (arrow).

later readmitted to the hospital because of coughing, low grade fever, and an atrioventricular (A-V) block in November, 1994. He had syncope caused by a complete A-V block. A-V block did not improve despite medication and cardioversion. A physical examination revealed no lymphadenopathy or hepatosplenomegaly. The results of a complete blood count, urinalysis, and a chemistry profile were all normal. Anti-human T-lymphotrophic virus type-1 and anti-human immunodeficiency virus antibodies were negative. Echocardiography, a computed tomographic (CT) scan and magnetic resonance imaging (MRI) of the chest showed a mass in the right atrial region near the right ventricular wall (Fig. 1a–c). A CT scan of the abdomen and pelvis revealed no mass or enlarged lymph node. A bone marrow examination showed no infiltration of the lymphoma cells. Therefore, a temporary pacemaker was inserted at a fixed rate of 70 beats per minute on November 19. Based on the above examinations, a cardiac tumor including malignant lymphoma was suspected, and thus an open biopsy of this tumor was performed. At operation, a white-grayish tumor invading the right atrial region and right ventricular wall and an enlarged mediastinal lymph node measuring approximately two cm in diameter, were recognized. These tumors were diagnosed to be malignant lymphoma, diffuse large cell type according to the Working Formulation [8] (Fig. 1d). An immunohistochemical examination was performed using the avidin-biotin complex method. Lymphoma cells were positive for CD19 (B4, Dichinson, Coulter Clone (CC), Hialeah, FL), CD20 (B1, CC), and HLA-DR (Dako, Glostrup, Denmark), but negative for T-cell antibodies including CD2 (T11, CC), CD3 (Leu 4, Becton-Dickinson, San Jose, CA), CD4 (OKT4, Ortho, Raritan, NJ), and CD8 (OKT3, Ortho, Raritan, NJ). These findings indicated that the tumor cells had a B-cell lineage. In situ hybridization with Epstein-Barr virus (EBV)-encoded RNA (EBER)-1 to detect EBV genomes, the method of which has been pre-

viously described [9], disclosed no EBV genomes in either the lymphoma cells or other cells.

The patient received one course of systemic chemotherapy, VEPA (vincristine, cyclophosphamide, prednisolone, and adriamycin). After the first course of VEPA, the A-V block disappeared. After four courses of VEPA, a CT scan showed about 75% reduction in the size of the mass. He was later transferred to the National Kyushu Cancer Center in January, 1995 to receive further therapy. He received radiation therapy (total doses 30 Gy) followed by four courses of THP-VEPA (vincristine, cyclophosphamide, prednisolone, and THP-adriamycin). After these treatments, a CT scan failed to show any trace of the tumor in his heart. Regarding the clinical course, he suffered from idiopathic interstitial pneumonia, but recovered after the administration of prednisolone. He is currently in complete remission at 34 months after the discontinuation of therapy.

DISCUSSION

Primary cardiac lymphoma, defined as that involving the heart and pericardium, is extremely rare. McAllister and Fenoglio [1] reported seven cases of 533 primary tumors of the heart (1.3%) in their series. We reviewed 26 cases of primary lymphoma reported since 1980, and 13 cases underwent an antemortem diagnosis of malignant lymphoma. In these 26 cases, there were five cases with lymph node and other organ involvement of lymphoma cells. Cairns et al. [10] mentioned that massive cardiac involvement with minimal lymphomatous infiltration of other sites is indicative of primary cardiac lymphoma, notwithstanding the diagnostic criteria of McAllister and Fenoglio [1]. Furthermore, when primary cardiac lymphoma reaches a certain size, it tends to disseminate, and the involvement of mediastinal lymph nodes, as well as the pleural effusion, most probably represent the local spread of the lymphoma [11–13]. In the present case, the lymphoma, which extended to the right atrium and ventricle, demonstrated one mediastinal lymph node at the operation. Although our case does not fulfill the criteria of primary cardiac lymphoma by McAllister and Fenoglio, this case is considered to be primary cardiac lymphoma, as the bulk of the tumor was restricted to the heart and pericardium.

Primary cardiac lymphoma is regarded to have a poor prognosis, because primary lymphomas are extremely rare and most patients often go untreated and are frequently only accurately diagnosed postmortem [10–12,14–19]. Furthermore, many patients who were diagnosed accurately before death could not be treated due to the aggressiveness of this lymphoma [2,14,15,20]. However, in 10 cases of primary cardiac lymphoma that were treated, six patients with a prolonged survival because of successful treatment have been recently reported [4–7,21]. Our case is also doing well and remains in complete remission 22 months after the completion of therapy. These cases thus indicate that when patients with primary cardiac lymphoma are diagnosed accurately and receive timely and appropriate therapy, many cases may be curable.

There have been some reports on the treatment of primary cardiac lymphoma related to a pacemaker [20], chemotherapy, including CHOP [5,6], BACOP [5], M-BACOD [7], vincristine and methyl prednisolone [22], CHOP [4], resection and chemotherapy [23], radiation therapy [21], and heart transplantation [24]. In these reports, a case which survived more than four years with chemotherapy (CHOP) is the longest known survivor [5]. However, no successfully treated case with primary cardiac lymphoma treated with a combination of chemotherapy and radiation to treat a complete A-V block controlled by a pacemaker has yet been reported.

The clinical manifestations of lymphoma in the heart are usually nonspecific or are insufficient to lead to a recognition of cardiac involvement antemortem. Our patient suffered from a complete A-V block, and the treatment for malignant lymphoma thus resulted in a complete disappearance of the A-V block. A complete heart block caused by tumor destruction of the conduction system is generally rare [20]. More common presenting symptoms associated with malignant tumors of the heart are congestive heart failure, pericardial effusion, and a superior vena cava obstruction [1,5,7,24]. There have been five reported cases demonstrating a complete A-V block in primary cardiac lymphoma [4,6,10,20,25]. Regarding the mechanism of A-V block, it has been described that lymphoma cells infiltrate the myocardium and then eventually damage the conduction system leading to a complete heart block [10,20,25]. Two patients with primary cardiac lymphoma demonstrating an A-V block were reported to still be alive [4,6]. Our present case is similar to the case reported by Nand [6].

A review of the literature indicates that most cases of primary cardiac lymphoma are large cell type. All cases examined by immunohistochemistry were B cell type except for one case [5]. A population of individuals that appear to be more susceptible to extranodal lymphomas are the immunosuppressed. Primary cardiac lymphoma has been described in patients with acquired immune deficiency syndrome [25,26]. Recently, the close relation between EBV and malignant lymphoma occurring in immunodeficient patients is well known. However, Ito and his colleagues [13] also reported two cases of primary cardiac lymphoma that appeared to have no association with EBV infection. In our case, no EBV genomes could be detected using in situ hybridization with EBER-1. From these findings, primary cardiac lymphoma is thus not considered to be related to EBV.

In summary, a tumor of the heart should be ruled out

employing useful modalities, when any cardiac signs or symptoms are demonstrated. The possibility of lymphoma should thus be included in the differential diagnosis in these patients. Our experience indicated that both an early diagnosis and appropriate therapy can result in a long survival in patients with primary cardiac lymphoma. Whenever a complete A-V block caused by an infiltration of lymphoma cells occurs, chemotherapy is thus considered to be the treatment of choice to control arrhythmia using a pacemaker.

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